

Supporting Information

Acceptorless Dehydrogenative Coupling using Ammonia: Direct Synthesis of N-Heteroaromatics from Diols Catalyzed by Ruthenium

Prosenjit Daw, Yehoshua Ben-David, and David Milstein*

Department of Organic Chemistry, Weizmann Institute of Science, Rehovot, 76100,
Israel.

* Corresponding Author E-mail: david.milstein@weizmann.ac.il.

Table of Contents

1) General procedure	S2
2) Experimental	S2
a) General procedure for the pyrazine formation reaction	S2
b) General procedure for the N-substituted pyrrole formation reaction	S3
Table S2. Optimization of pyrrole formation from alcohols and ammonia	S4
Table S3. Pyrrole formation from alcohols and ammonia	S5-6
3) Treatment of 1,4-diol derivatives with catalyst 1 and ammonia with no added primary alcohol	S7
4) Treatment of 1,4-diol derivatives and 1-hexanol with catalyst 1 and ammonia	S7-8
5) Synthesis of complex 3	S9-10
6) Reaction of complex 1 and benzyl alcohol in presence of ammonia	S11
7) Reaction of complex 2 and benzyl alcohol in presence of ammonia	S12
8) Proposed mechanism for alcohol amination	S13
9) Reaction of 2,5-hexanediol and 1-hexylamine with complex 2	S14
10) Reaction of 2,5-dimethylpyrrole and 1-hexanol with complex 2	S14
11) ^1H and ^{13}C NMR data of isolated pyrazines	S15
12) ^1H and ^{13}C NMR spectra of isolated pyrazines	S16-20
13) ^1H NMR spectra of synthesized pyrroles with mesitylene as internal standard	S21-22
14) Procedure for the detection of H_2	S23
15) References	S24

1. General Procedure

All experiments with metal complexes and phosphine ligands were carried out under an atmosphere of purified nitrogen in a Vacuum Atmospheres glovebox equipped with a MO 40-2 inert gas purifier or using standard Schlenk techniques under argon atmosphere. All solvents were reagent grade or better. Non-deuterated solvents were dried over sodium/benzophenoneketyl (tetrahydrofuran, n-pentane, and toluene), and distilled under argon atmosphere. All solvents were degassed with argon and kept in the glove box over activated 4Å molecular sieves. Deuterated solvents were purchased from Aldrich, purged with argon and stored over activated 4Å molecular sieves in the glove box. ^1H , and ^{13}C NMR spectra were recorded using Bruker AMX-300, 400 and 500 NMR spectrometer. All spectra were recorded at 298 K, unless otherwise noted. ^1H NMR and $^{13}\text{C}\{^1\text{H}\}$ NMR chemical shifts are reported in ppm downfield from tetramethylsilane and referenced to the residual signals of an appropriate deuterated solvent. $^{31}\text{P}\{^1\text{H}\}$ NMR chemical shifts are reported in ppm downfield from H_3PO_4 and referenced to an external 85% solution of phosphoric acid in D_2O . NMR spectroscopy abbreviations: br, broad; s, singlet; d, doublet; m, multiplet. GCMS was carried out on HP 6890 (flame ionization detector and thermal conductivity detector) and HP 5973 (MS detector) instruments equipped with a 30 m column (Restek 5MS, 0.32 mm internal diameter) with a 5% phenylmethylsilicone coating (0.25 mm) and helium as carrier gas. Most of the commercially available reagents were used as received.

Ligand Acr-CH₂PNP^{iPr} and the ruthenium complexes **1**, **2** were prepared according to literature procedures.^{1,2}

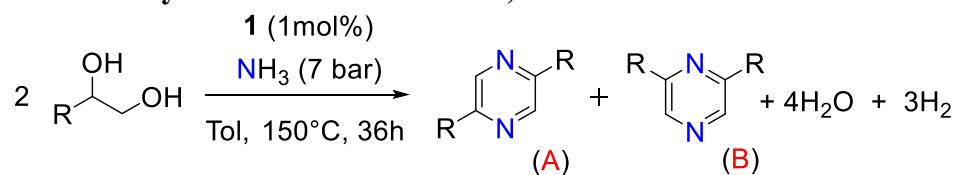
2. Experimental

a) General procedure for the pyrazine formation reaction:

For Table 1: To a solution of 0.01 mmol catalyst **1** in 2 mL dry toluene in a 100 ml Fisher Porter tube was added 1 mmol of 1,2-diol substrate under N_2 atmosphere. The tube was closed and was taken out from the box and purged with 2 bar of ammonia for 3 times and finally pressurized with 7 bar of ammonia. The reaction mixture was stirred at 150°C for 36h, cooled down to room temperature and the ammonia pressure was released in the

hood. The reaction products were analyzed by GC-MS and ^1H NMR, and the pyrazines were isolated after column chromatography.

Table S1. Pyrazine formation from 1,2-diols and ammonia^a



Entry	Substrate	Products	Mass	R.T.	Yield ^b [A/B]
1			192	14.31	99
				14.58	[65/35]
2			304	19.84	99
				20.19	[50/50]
3			416	25.91	99
				27.14	[58/42]
4			232	20.02	100
				20.34	[68/32]
5 ^c			136	10.75	72
6 ^c			108	8.28	42
7 ^c			136	10.73	85 (15) ^d
8			188	16.51	95 (5) ^d

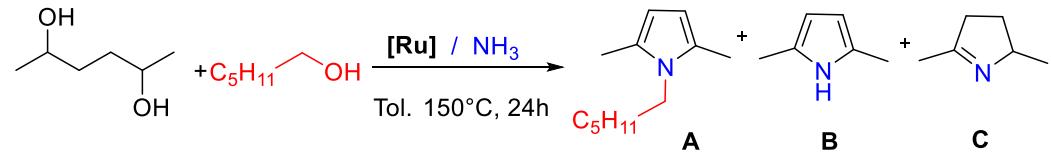
^aReaction conditions: Catalyst **1** (0.01 mmol), 1,2-diol (1 mmol), 150°C, 36h, toluene (2ml), ^bIsolatd yield. ^cGC-MS yield with mesitylene as internal standard.

^dhydrogenated product. R.T.= Retention Time

b) General procedure for the N-substituted pyrrole formation reaction (for Table S2): To a solution of 0.01 mmol catalyst **1** in 0.5 mL (or 2 mL for entry 1, 2) of dry toluene in a 100 ml Fisher Porter tube was added the specified amounts of 2,5-hexanediol and 1-hexanol under N₂ atmosphere. The tube was closed and was taken out from the box and purged with 2 bar of ammonia 3 times and finally pressurized with 7 bar of ammonia.

The reaction mixture was stirred at 150°C for 24h, cooled down to room temperature and the ammonia pressure was released in the hood. The reaction products were analyzed by GC-MS and ¹H NMR to determine the yield with mesitylene as internal standard.

Table S2. Optimization of pyrrole formation from alcohols and ammonia^a



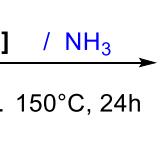
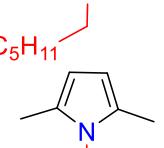
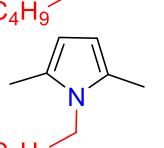
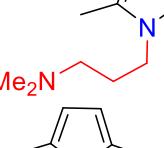
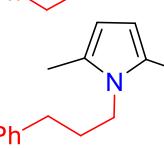
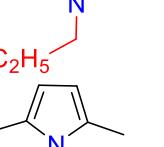
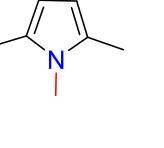
Entry	[Ru] (mol%)	Toluene (mL)	2,5-Hexanediol (mmol)	1-Hexanol (mmol)	Yield (%)		
					A	B	C
1	1 (2)	2	0.5	0.5	17	18	35
2	1 (2)	2	0.5	1	42	8	46
3	1 (1)	0.5	1	1	63	11	24
4	1 (1)	0.5	1	2	90	8	2
5	1 (0.5)	0.5	1	1	74	4	19
6 ^c	1 (1)	-	1	2	30	12	46
7 ^d	2 (1)	0.5	1	2	50	12	32
8 ^e	2 (1)	0.5	1	2	68	12	18

^aReaction conditions: Catalyst **1** (as mentioned), 2,5-hexanediol (as mentioned), 1-hexanol (as mentioned), ammonia (7 bar), 150°C, 24h, toluene (as mentioned), ^bGC-MS for detection and ¹H NMR for yield with mesitylene as internal standard. ^cneat condition, solvent free. ^dCatalyst **2** [Ru(H-AcrCH₂PNP^{iPr})H(CO)], (0.01 mmol). ^eCatalyst **2** [Ru(H-AcrCH₂PNP^{iPr})H(CO)], (0.01 mmol) and NH₄Cl (2 mol%).

For Table 3 and S3:

To a solution of 0.01 mmol catalyst **1** in 0.5 mL dry of toluene in a 100 ml Fisher Porter tube were added 1 mmol of 2,5-hexanediol and 2 mmol of primary alcohol (4 mmol for low boiling primary alcohols, Table S3, entries 8-10) under N₂ atmosphere. The tube was closed and was taken out from the box and purged with 2 bar of ammonia 3 times and finally pressurized with 7 bar of ammonia. The reaction mixture was stirred at 150°C for 24h, cooled down to room temperature and the ammonia pressure was released in the hood. The reaction products were analyzed by GC-MS and ¹H NMR to determine the yield with mesitylene as internal standard.

Table S3. Pyrrole formation from alcohols and ammonia^a

Entry	alcohol (mmol)	Product	Mass	Rt in GCMS			Yield (%)
				A	B	C	
1	<chem>C5H11CH2OH</chem>		179	13.96	90	8	2
2	<chem>C7H15CH2OH</chem>		207	15.61	83	7	9
3	<chem>C4H9CH2OH</chem>		165	13.06	76	11	10
4	<chem>C3H7CH2OH</chem>		151	12.14	77	13	10
5	<chem>Me2NCH2CH2CH2OH</chem>		180	13.89	74	17	8
6	<chem>c1ccccc1CH2OH</chem>		199	15.98	76	6	18
7	<chem>c1ccccc1CH2CH2OH</chem>		213	17.11	74	5	20
8 ^c	<chem>C2H5CH2OH</chem>		137	11.06	74	19	5
9 ^c	<chem>CH3CH2OH</chem>		123	10.03	71	20	7
10 ^c	<chem>CH3OH</chem>		109	9.50	29	10	55

11			185	15.04	57	4	36
12			199	15.91	48	8	45
13			245	18.11	13	-	-
14			186	15.88	69	12	14
15			175	13.59	84	9	5

^aReaction conditions: Catalyst **1** (0.01 mmol), 2,5-hexanediol (1 mmol), primary alcohol (2 mmol), ammonia (7 bar), 150°C, 24h, toluene (0.5 mL), ^bGC-MS for detection and ¹H NMR yield with mesitylene as internal standard. ^cPrimary alcohol (4 mmol).

3. Treatment of 1,4-diol derivatives with catalyst **1** and ammonia with no added primary alcohol

To a solution of 0.01 mmol catalyst **1** in 2 mL dry of toluene in a 100 ml Fisher Porter tube was added 1 mmol of 1,4-diols under N₂ atmosphere. The tube was closed and was taken out from the box and purged with 2 bar of ammonia for 3 times and finally pressurized with 7 bar of ammonia. The reaction mixture was stirred at 150°C for 24h, cooled down to room temperature and the ammonia pressure was released in the hood. The reaction products were analyzed by GC-MS and ¹H NMR to determine the yield with mesitylene as internal standard. 1,4-butanediol used as substrate yielded pyrrolidine as the single product and 2,5-hexanediol afforded a mixture of 85% yield of 2,5-dimethyl-1-pyrroline and 15% yield of the 2,5-dimethylpyrrole. Use of 1-phenyl-1,4-pentanediol afforded 60% of 2-methyl-5-phenyl-1-pyrroline and 40% yield of the 2-methyl-5-phenylpyrrole.

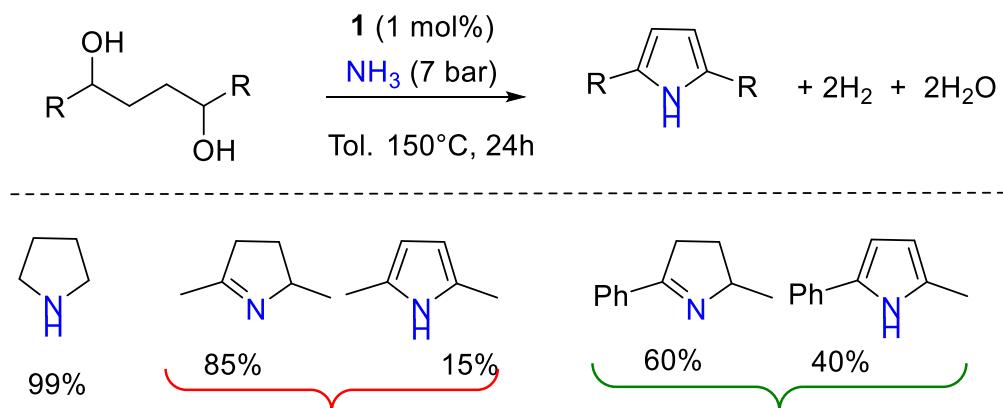


Figure S1. Reaction of 1,4-butanediol substrates with ammonia in presence of catalyst **1**

4. Treatment of other 1,4-diol derivatives and 1-hexanol with catalyst **1** and ammonia:

To a solution of 0.01 mmol catalyst **1** in 0.5 mL dry of toluene in a 100 ml Fisher Porter tube was added 1 mmol of 1,4-diols and 2 mmol of 1-hexanol under N₂ atmosphere. The tube was closed and was taken out from the box and purged with 2 bar of ammonia for 3

times and finally pressurized with 7 bar of ammonia. The reaction mixture was stirred at 150°C for 24h, cooled down to room temperature and the ammonia pressure was released in the hood. The reaction products were analyzed by GC-MS and ¹H NMR to determine the yield with mesitylene as internal standard.

The treatment of 1,4-butanediol with 1-hexanol and ammonia N-hexylpyrrolidine as the coupling product (40%) along with N-hexylpyrrole (10%) and pyrrolidine was observed. Under the optimized conditions, reaction of 1-phenyl-1,4-pentanediol and 1-hexanol with ammonia afforded 44% yield of the 1-hexyl-2-phenyl-5-methyl pyrrole and 37% of the 2-phenyl-5-methyl pyrrole and 37% 2-methyl-5-phenyl-1-pyrroline was formed and 1-hexanol fully converted to 1-hexylamine and dihexylamine. 1-hexyl-2,5-diphenyl pyrrole was formed in 10% yield from the 1,4-diphenyl-1,4-butanediol and 1-hexanol with 2,5-diphenylpyrrole as the major product.

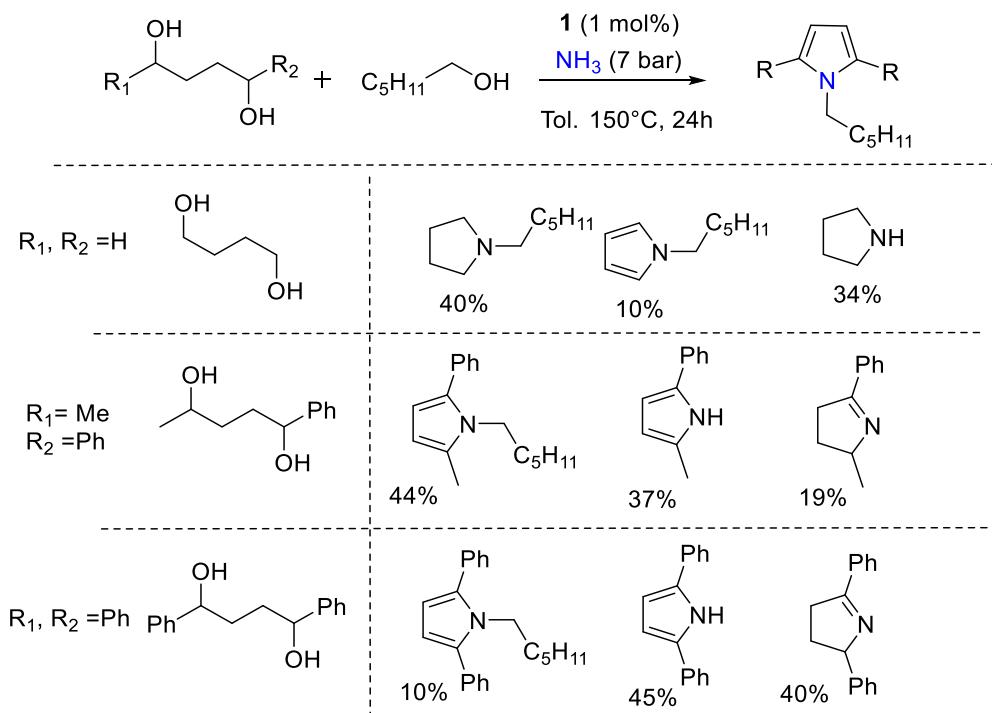


Figure S2. Reaction of 1,4-butanediol substrates and 1-hexanol with ammonia in presence of catalyst **1**

5. Synthesis of complex 3:

14 mg (0.02 mmol) of Ru(H-AcrCH₂PNPⁱPr)H(CO) (**2**) was taken in J Young NMR tube and dissolved in 0.5 mL d₈-toluene under N₂ atmosphere. The gas was removed by freeze pump thaw and charged with 1 bar of NH₃. An immediate change of the color from orange to light yellow took place, indicating that NH₃ was bounded to the Ru center. ¹H NMR (Tol-d₈, 500 MHz): δ = -14.8 (t, *J*= 23.4Hz, 1H, Ru-H), 0.23 (br, 3H, NH₃), 0.89 (m, 6H), 0.97 (m, 6H), 1.19 (m, 2H), 1.25 (m, 6H), 1.36 (m, 6H), 2.22 (m, 2H), 2.64 (m, 2H), 3.15 (d, *J*=12.1Hz, 2H), 3.49 (d, *J*=16.2Hz, 1H), 3.86 (d, *J*=16.5Hz, 1H), 6.84-6.87 (m, 3H), 7.06-7.08 (m, 3H). ³¹P{¹H} NMR (Tol-d₈, 202 MHz): δ = 77.28

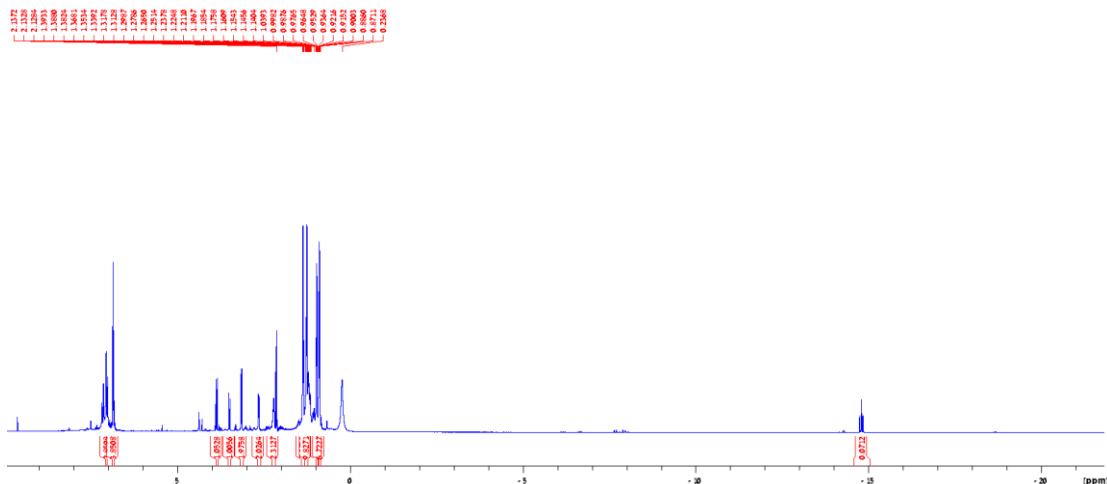


Figure S3. ¹H NMR spectrum of complex **3** in tol-d₈

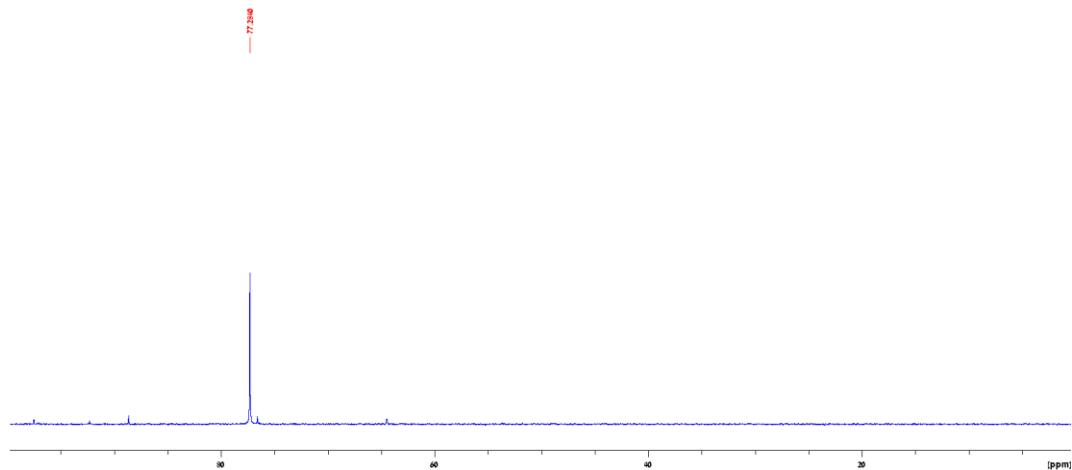


Figure S4. ³¹P{¹H} NMR spectrum of complex **3** in tol-d₈

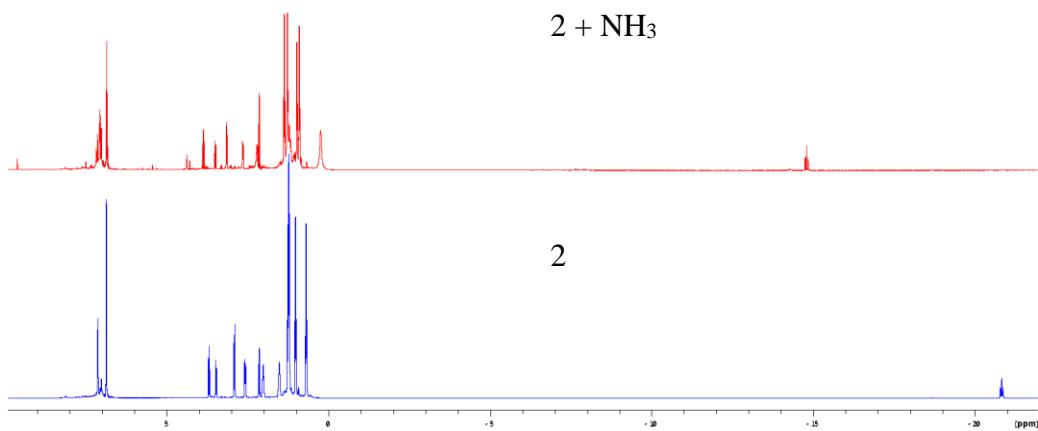


Figure S5. ¹H NMR spectrum for the reaction of complex **2** and NH₃ in tol-d₈

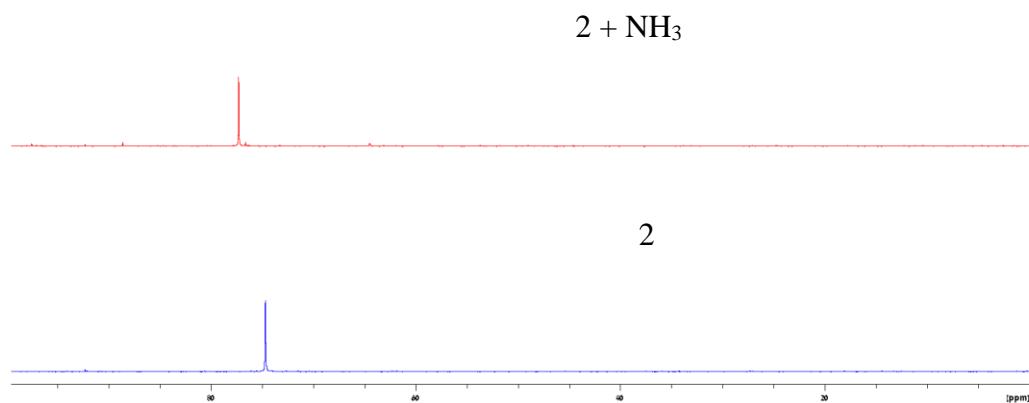


Figure S6. ³¹P{¹H} NMR spectrum for the reaction of complex **2** and NH₃ in tol-d₈

6. Reaction of complex **1** and benzyl alcohol in presence of ammonia:

7 mg (0.01 mmol) of Ru(AcrCH₂PNPⁱPr)HCl(CO) (**1**) was placed in a high pressure NMR tube and dissolved in 0.5 mL C₆D₆ under N₂ atmosphere. 5 equivalent of benzyl alcohol was added to the NMR tube and it was taken out from the glove box and purged with 2 bar of ammonia 3 times and finally pressurized with 7 bar of ammonia. The NMR tube was heated at 150°C for 24h, forming benzyl amine. The formed ammonia-bound complex **3** was observed after the reaction by ³¹P NMR at 77.28 ppm and in ¹H NMR the Ru-H appears at -14.8 ppm.

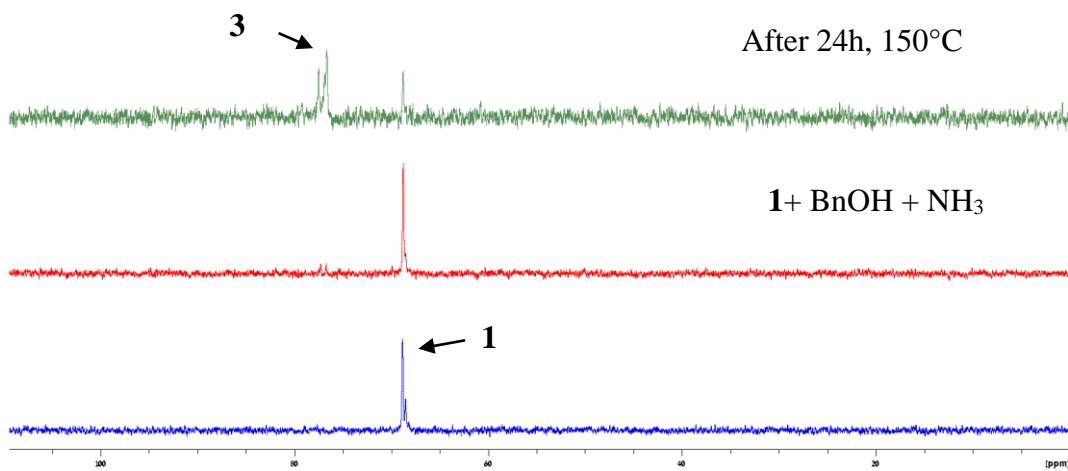


Figure S7. ³¹P{¹H} NMR spectrum for the reaction of **1** and benzyl alcohol with NH₃ in C₆D₆

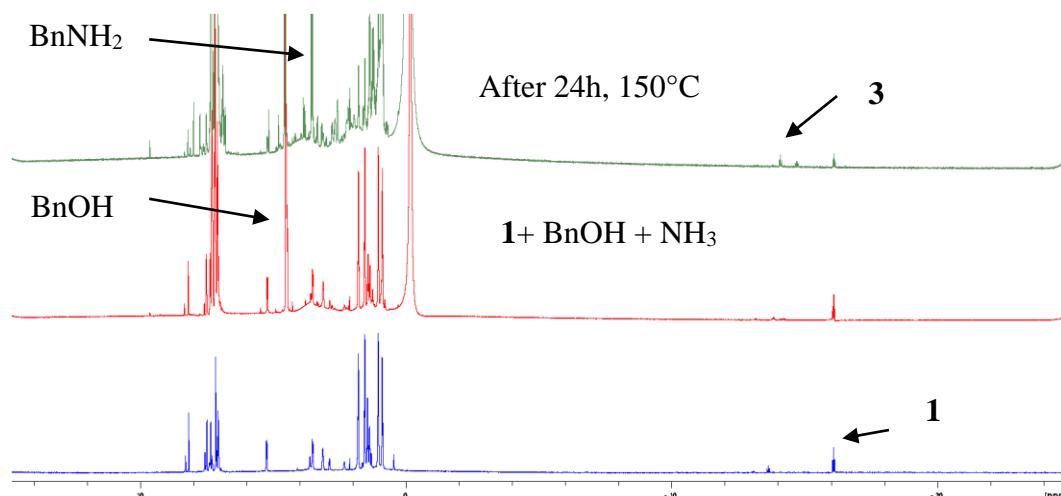


Figure S8. ¹H NMR spectrum for the reaction of **1** and benzyl alcohol with NH₃ in C₆D₆

7. Reaction of complex **2** and benzyl alcohol in presence of ammonia:

To a solution of 7 mg (0.01 mmol) of Ru(H-AcrCH₂PNPⁱPr)H(CO) (**2**) in 0.5 mL C₆D₆ in a high pressure NMR tube under N₂ were added 5 equivalents of benzyl alcohol. The reaction mixture was taken out of the glove box and purged with 2 bar of ammonia 3 times and finally pressurized with 7 bar of ammonia. Immediate formation of complex **3** was observed after addition of ammonia. The NMR tube was heated at 150°C for 24h. N-benzylidenebenzylamine formation was observed and the ammonia-bound complex **3** was still present.

Under the optimized condition (1 mmol of benzyl alcohol, 0.01 mmol of catalyst **2**, 2 ml toluene, 7 bar NH₃, 150°C, 24h), full conversion of benzyl alcohol to benzyl amine (90%) and N-benzylidenebenzylamine (10%) was observed.

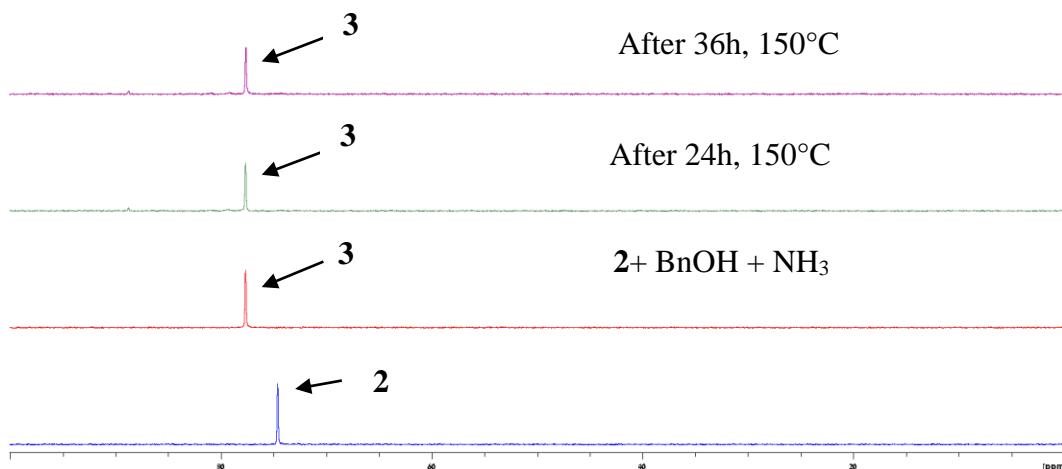


Figure S9. $^{31}\text{P}\{^1\text{H}\}$ NMR spectrum of the reaction of **1** and benzyl alcohol with NH₃ in C₆D₆

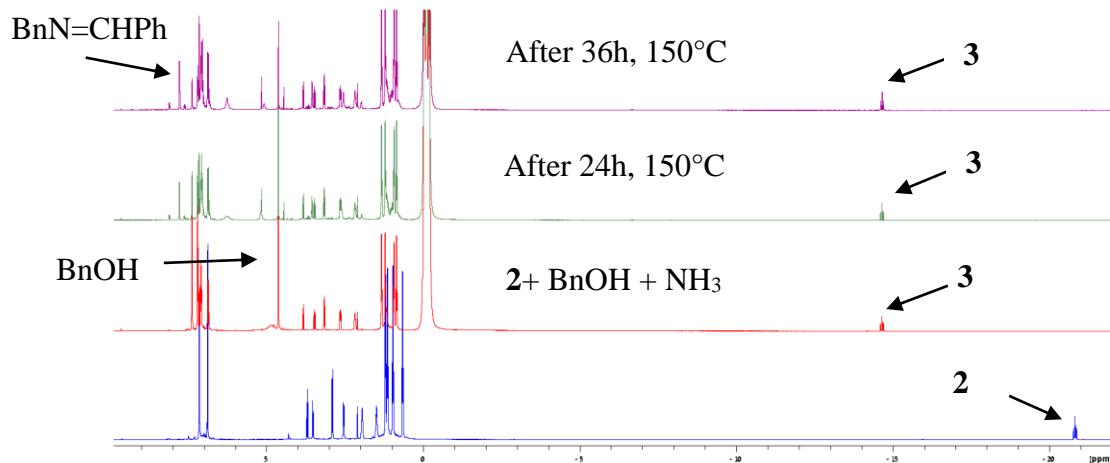
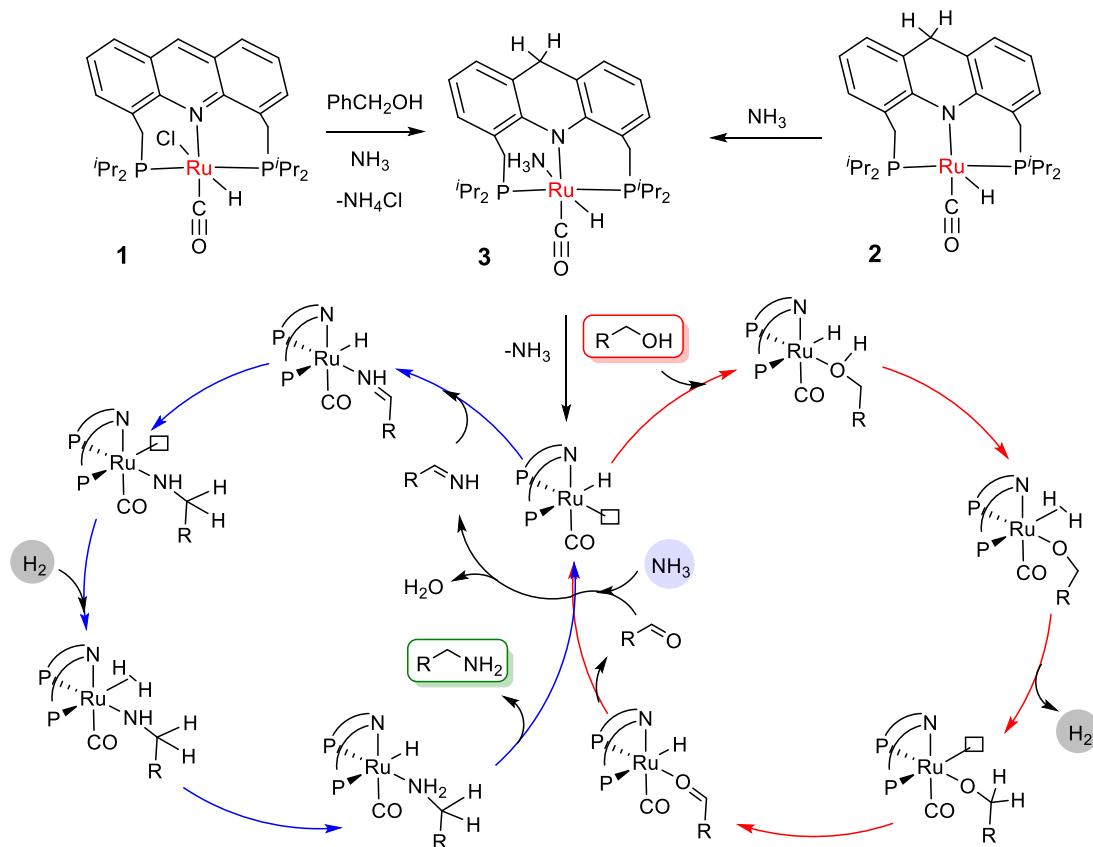


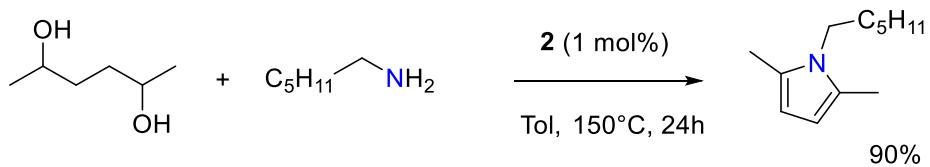
Figure S10. ^1H NMR spectrum for the reaction of **2** and benzyl alcohol with NH_3 in C_6D_6

8. Proposed mechanism for alcohol amination



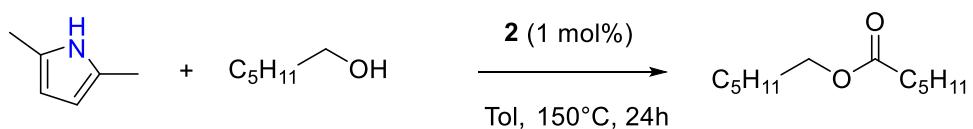
9. Reaction of 2,5-hexanediol and 1-hexylamine with complex 2

To a solution of 0.005 mmol catalyst **2** in 2 mL dry of toluene in a 50 ml Teflon Schlenk tube was added 0.5 mmol of 2,5-hexanediol and 0.5 mmol 1-hexylamine under N₂ atmosphere. The reaction mixture was stirred at 150°C for 24h, cooled down to room temperature and the formed hydrogen was released in the hood. The reaction products were analyzed by GC-MS with mesitylene as internal standard. N-hexyl-2,5-dimethylpyrrole was afforded with 90% yield.

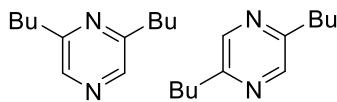


10. Reaction of 2,5-dimethylpyrrole and 1-hexanol with complex 2

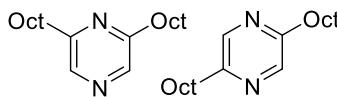
To a solution of 0.005 mmol catalyst **2** in 2 mL dry of toluene in a 50 ml Teflon Schlenk tube was added 0.5 mmol of 2,5-dimethylpyrrole and 0.5 mmol 1-hexanol under N₂ atmosphere. The reaction mixture was stirred at 150°C for 24h, cooled down to room temperature and the formed hydrogen was released in the hood. The reaction products were analyzed by GC-MS with mesitylene as internal standard. Hexyl hexanoate (72%) was observed as the major product with unreacted 2,5-dimethylpyrrole and N-hexyl-2,5-dimethylpyrrole was not formed.



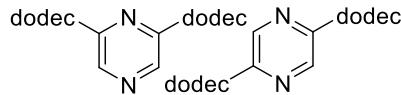
11. ^1H and ^{13}C NMR data of isolated pyrazines:



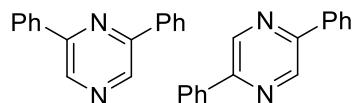
^1H NMR (500 MHz, CDCl_3) δ : 0.96 (t, $J = 7.62\text{Hz}$, 3H), 1.39-1.43 (m, 2H), 1.71-1.74 (m, 2H), 2.79 (t, $J = 7.93\text{Hz}$, 2H), 8.26, 8.32 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): 13.8, 13.8, 22.4, 22.4, 31.6, 31.8, 34.7, 35.3, 141.3, 143.3, 154.6, 156.8.



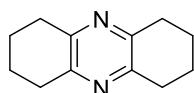
^1H NMR (500 MHz, CDCl_3) δ : 0.97 (t, $J = 6.57\text{Hz}$, 3H), 1.36-1.43 (m, 10H), 1.81-1.83 (m, 2H), 2.89 (t, $J = 7.53\text{Hz}$, 2H), 8.38, 8.47 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): 14.0, 22.6, 29.2, 29.2, 29.3, 29.3, 29.4, 29.5, 29.6, 31.8, 34.9, 35.4, 141.1, 143.0, 154.6, 156.8.



^1H NMR (500 MHz, CDCl_3) δ : 0.90 (t, $J = 7.06\text{ Hz}$, 3H), 1.27-1.33 (m, 18H), 1.74-1.78 (m, 2H), 2.85 (t, $J = 7.57\text{Hz}$, 2H), 8.33, 8.44 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): 14.1, 22.7, 29.2, 29.3, 29.3, 29.4, 29.5, 29.6, 29.6, 29.7, 31.9, 142.4, 154.6.



^1H NMR (500 MHz, CDCl_3) δ : 7.52-7.57 (m, 3H), 8.09 (d, $J = 7.56\text{Hz}$, 1H), 8.18 (d, $J = 7.65\text{Hz}$, 1H), 9.00, 9.01 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): 126.8, 127.0, 128.9, 129.0, 129.1, 129.8, 130.0, 133.3, 141.2, 150.7.



^1H NMR (500 MHz, CDCl_3) δ : 1.92 (br, 2H), 2.93 (br, 2H); $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz, CDCl_3): 22.5, 31.2, 149.3.

12. ^1H and ^{13}C NMR spectra of isolated pyrazines:

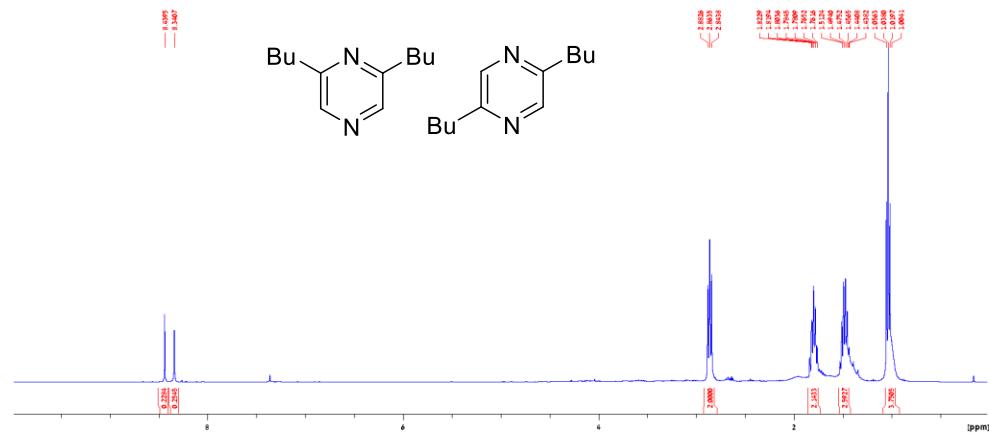


Figure S11. ^1H NMR of dibutylpyrazine

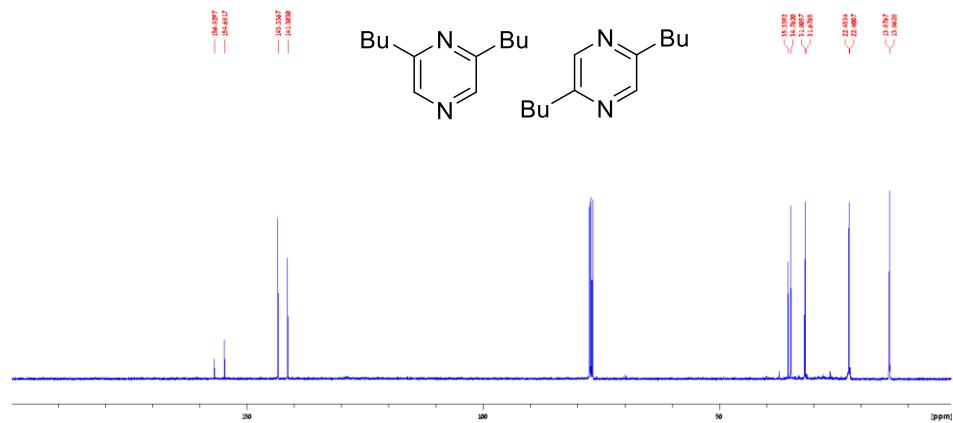


Figure S12. $^{13}\text{C}\{\text{H}\}$ NMR of dibutylpyrazine

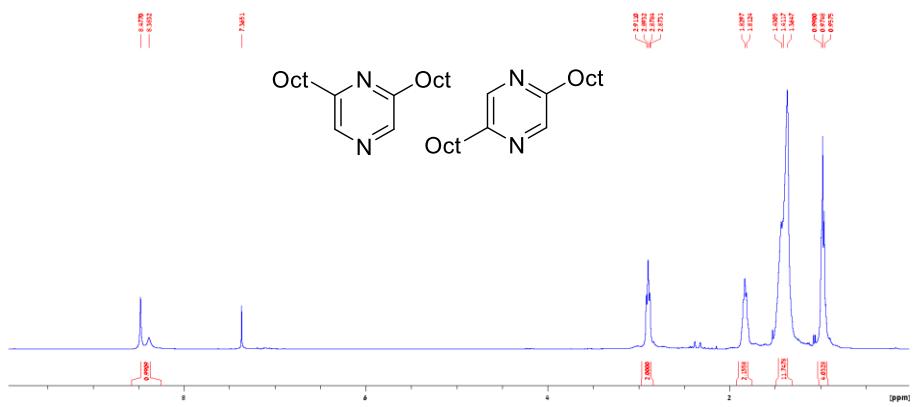


Figure S13. ^1H NMR of dioctylpyrazine

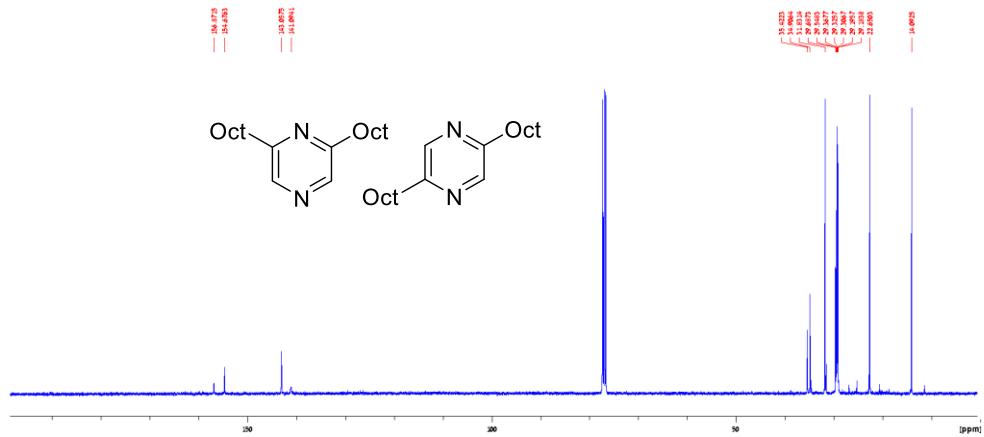


Figure S14. $^{13}\text{C}\{\text{H}\}$ NMR of dibutylpyrazine

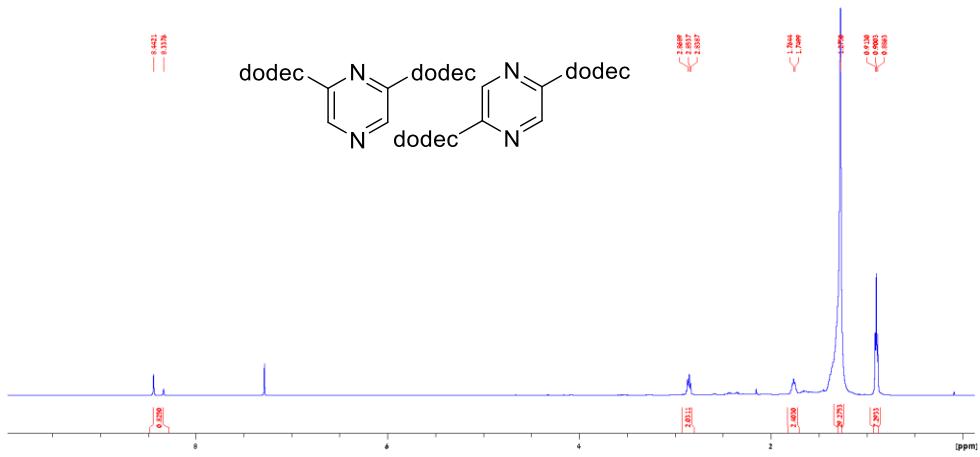


Figure S15. ^1H NMR of didodecanepyrazine

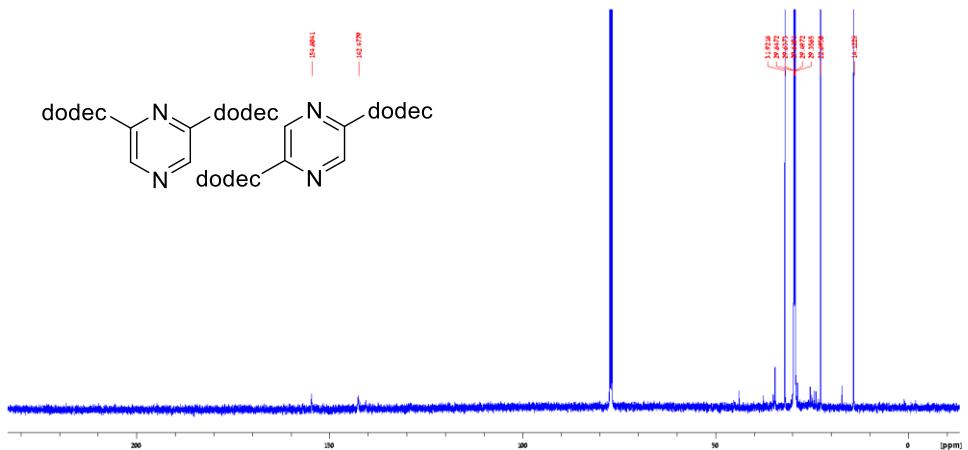


Figure S16. $^{13}\text{C}\{^1\text{H}\}$ NMR of didodecanepyrazine

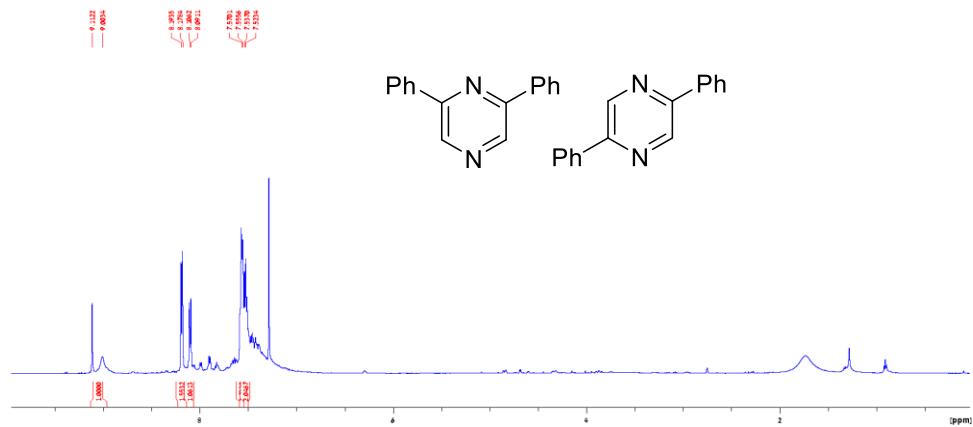


Figure S17. ^1H NMR of diphenylpyrazine

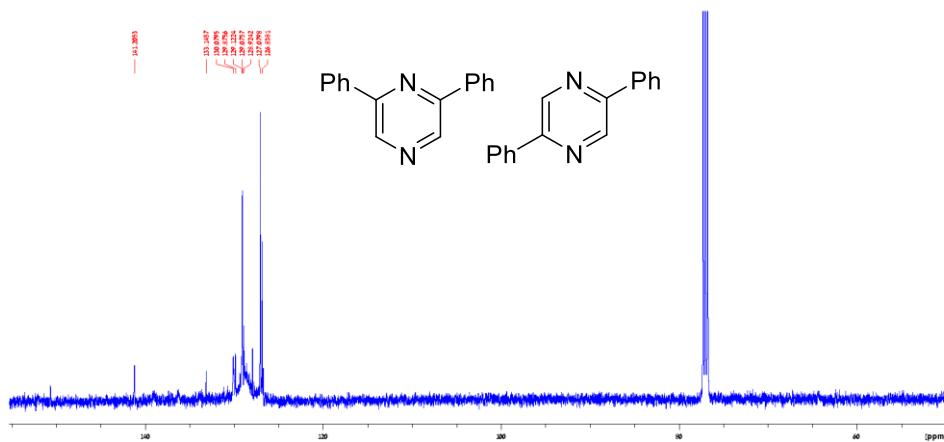


Figure S18. $^{13}\text{C}\{^1\text{H}\}$ NMR of diphenylpyrazine

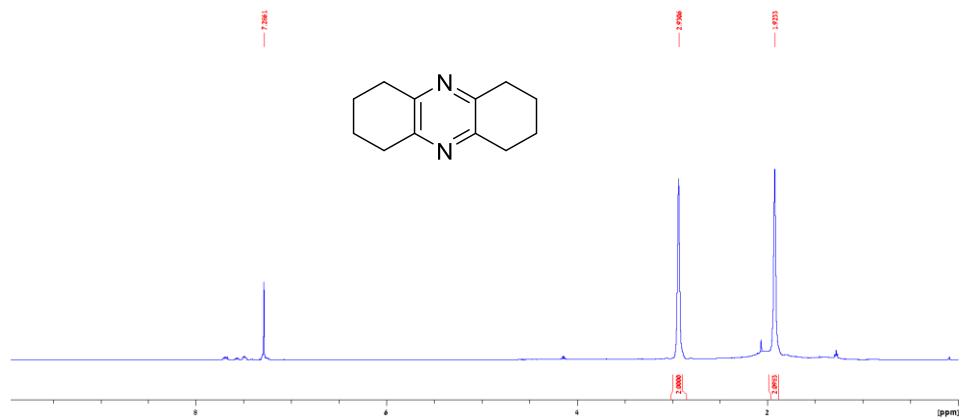


Figure S19. ^1H NMR of 1,2,3,4,6,7,8,9-octahydrophenazine

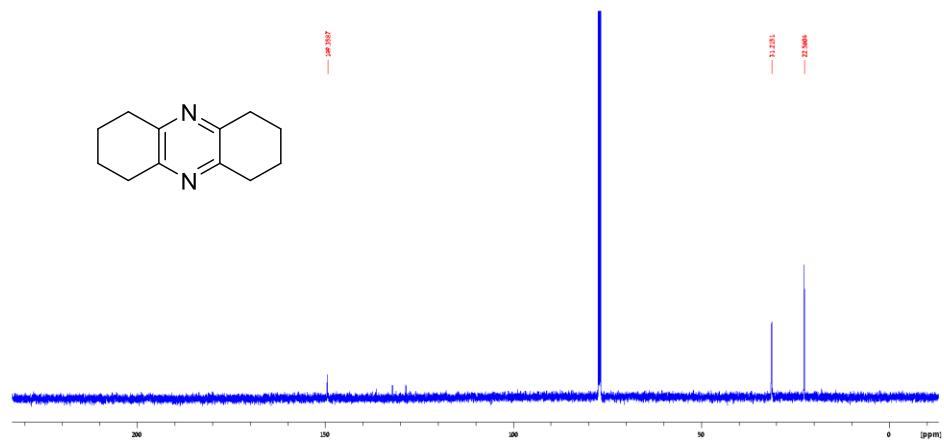


Figure S20. $^{13}\text{C}\{^1\text{H}\}$ NMR of 1,2,3,4,6,7,8,9-octahydrophenazine

13. ^1H NMR spectra of synthesised pyrroles with mesitylene as internal standard:

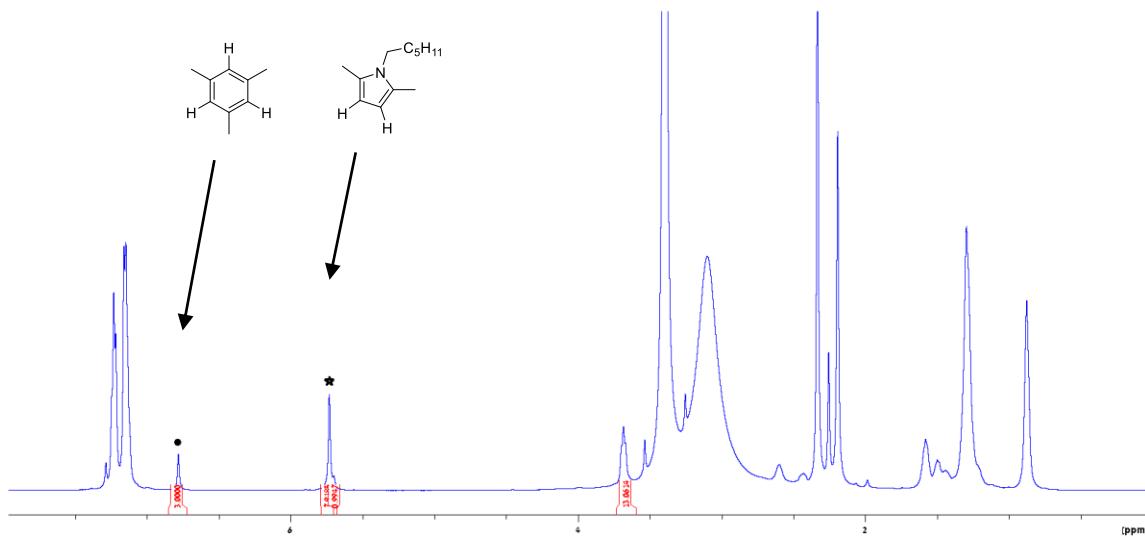


Figure S21. ^1H NMR of N-hexyl-2,5-dimethylpyrrole

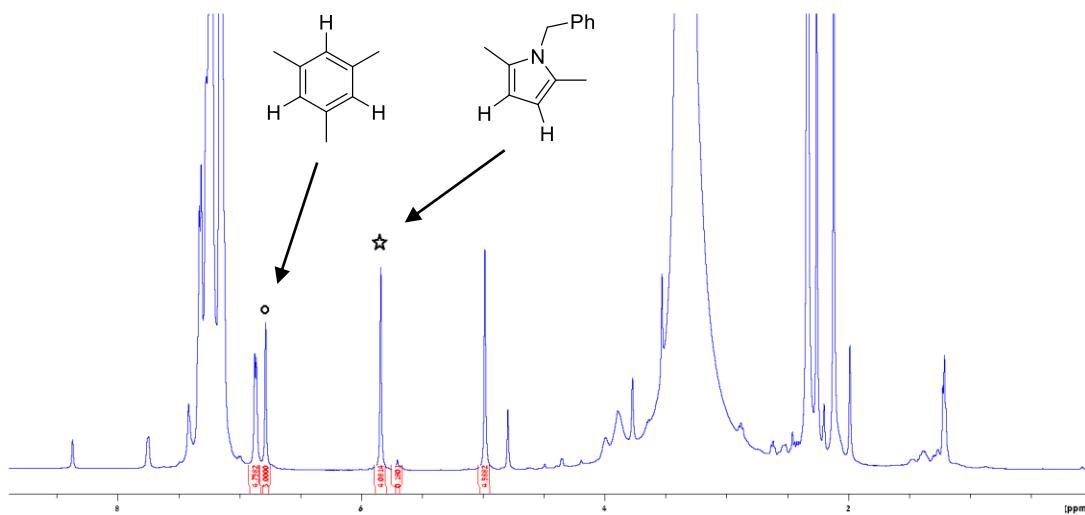


Figure S22. ^1H NMR of N-benzyl-2,5-dimethylpyrrole

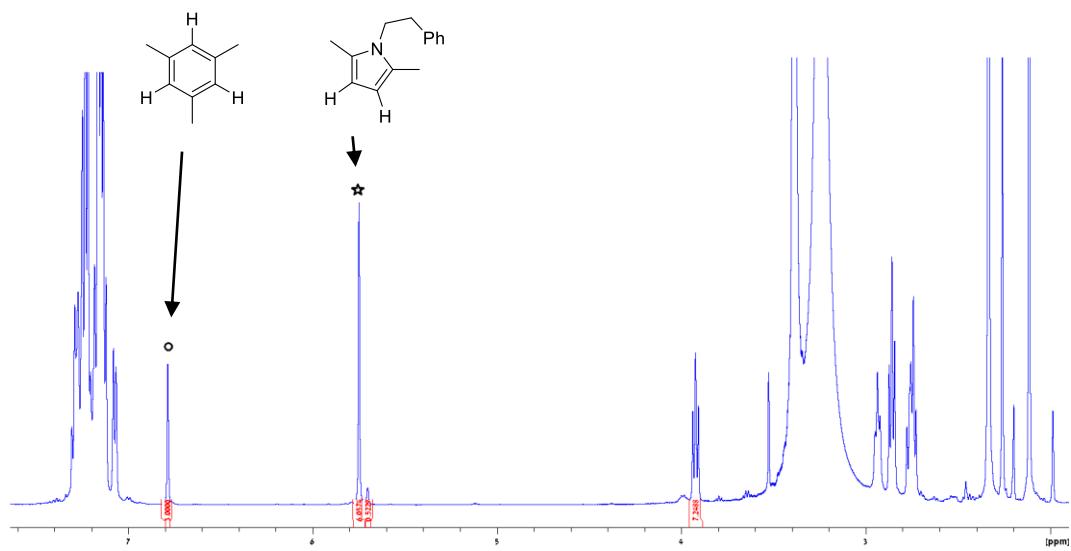


Figure S23. ¹H NMR of N-(2phenylethyl)-2,5-dimethylpyrrole

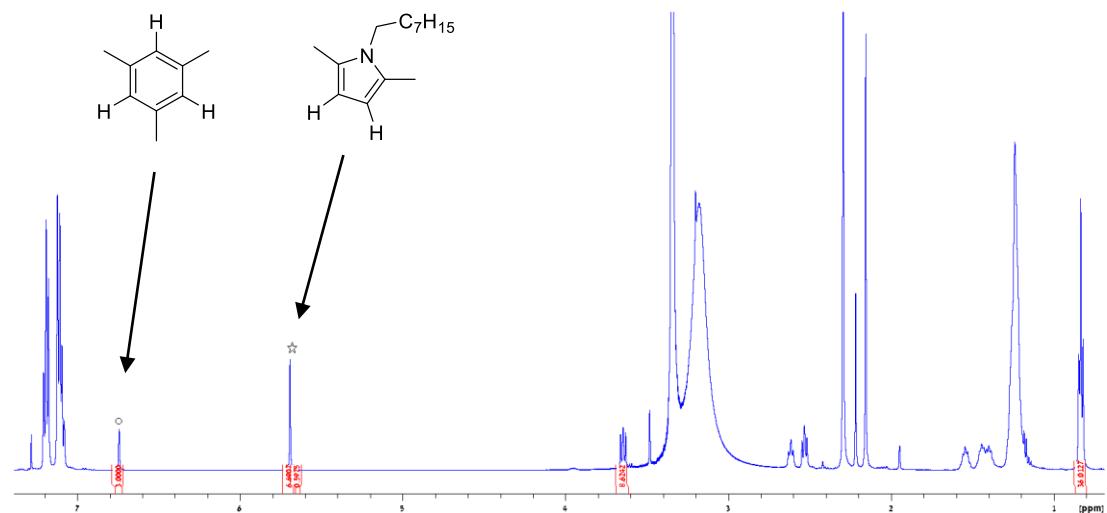


Figure S24. ¹H NMR of N-octyl-2,5-dimethylpyrrole

14. Procedure for the detection of H₂:

To a solution of 0.01 mmol catalyst **1** in 0.5 mL dry of toluene in a 100 ml Fisher Porter tube were added 1 mmol of 2,5-hexanediol and 2 mmol of 1-hexanol under N₂ atmosphere. The tube was closed and was taken out of the box, purged with 2 bar of ammonia 3 times and finally pressurized with 7 bar of ammonia. The reaction mixture was stirred at 150°C for 24h and then cooled down to room temperature, followed by further cooling with liq. N₂ to freeze the reaction mixture including gaseous ammonia. The remaining gas mixture was injected into a GC instrument equipped with a thermal conductivity detector, showing formation of H₂.

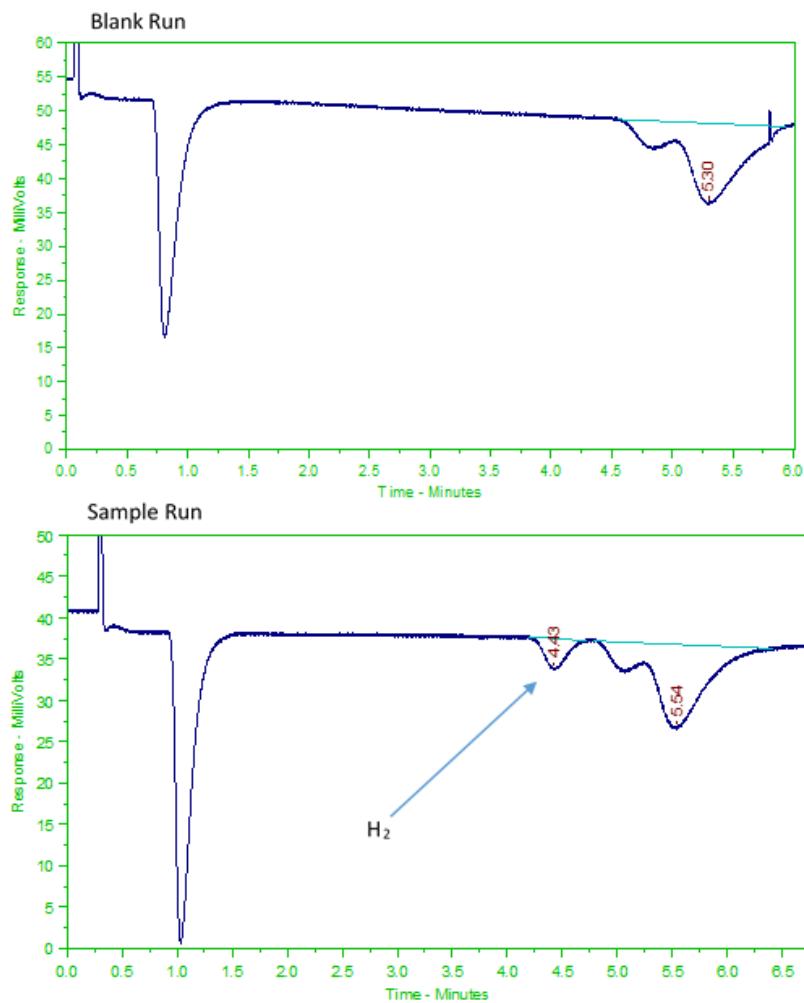


Figure S25. Thermal conductivity detector GC spectrum for the gas phase analysis after the pyrrole formation reaction

15. REFERENCES

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- (2) Gellrich, U.; Khusnutdinova, J. R.; Leitus, G. M.; Milstein, D. Mechanistic Investigations of the Catalytic Formation of Lactams from Amines and Water with Liberation of H₂. *J. Am. Chem. Soc.*, **2015**, *137*, 4851–4859.